OIPE
NOV 18 2002
PATENT & TRADEMARK OFFICE

CLEAN VERSION OF AMENDED SPECIFICATION PARAGRAPHS

METHOD OF IDENTIFYING INHIBITORS OF TOPOISOMERASE DNA RELIGATION
Applicant: Frederic Bushman et al.
Serial No.: 09/583,342

Please replace the paragraph at page 3, lines 10-27 with the following paragraph:

B1

The present invention provides high-throughput methods of screening compounds capable of modulating topoisomerase activity by incubating at least a first nucleic acid, a topoisomerase and a potential topoisomerase-modulating compound, wherein the nucleic acid is operatively associated with at least one tag, and assaying for nucleic acid religation. It is then possible to measure the level of substrate nucleic acid religation activity in the presence and absence of the topoisomerase-modulating compound, wherein the level of religation activity is inversely proportional to the effectiveness of the topoisomerase-inhibitory compound. The nucleic acid may be single-stranded or double-stranded DNA, or single-stranded or double-stranded RNA. The tag may be a detection tag or an affinity tag. The method may involve incubating at least a first nucleic acid and a second nucleic acid, and the first nucleic acid may be operatively associated with an affinity tag, and the second nucleic acid may be operatively associated with a detection tag. The topoisomerase-modulating compound may be a topoisomerase inhibitor or an activator. The topoisomerase may be a Type I, Type II, Type III or Type IV topoisomerase. The screening assay may be performed on a solid support or in a liquid phase. The nucleic acid and topoisomerase may be covalently complexed, wherein the topoisomerase retains its religation activity.

Please replace the paragraph at page 4, line 7-11 with the following paragraph:

B2

The present invention also provides a high-throughput method of screening compounds capable of modulating nucleic acid-modifying enzymatic activity by incubating at least a first nucleic acid, a nucleic acid-modifying enzyme and a potential enzyme-modulating compound, wherein the nucleic acid has at least one tag, and assaying for nucleic acid religation or cleavage.